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REMARKS

Favorable reconsideration is respectfully requested in view of the above amendments and following remarks. Claim 15 has been amended editorially. No new matter has been added. Claims 19-22 have been withdrawn. Applicants suggest that claims 19-22 should be reinstated if claim 1 is allowable. Claims 1-18 are pending.

Claim Objections

Claim 15 is objected to because of informalities. Claim 15 has been amended, taking the issues noted in the objection into account.

Withdrawal of the objection is respectfully requested.

Claim rejections - 35 U.S.C. § 103

Claims 1-6 are rejected under 35 USC 103(a) as being unpatentable over Garg et al. (WO 03/063825) in view of Fulbreth et al. (US 5,151,433). Applicants respectfully traverse the rejection.

Claim 1 is directed to a stabilized pharmaceutical solid composition. Claim 1 requires the stabilized pharmaceutical solid composition to include an ACE inhibitor and meglumine. Advantageously, the composition according to claim 1 show enhanced stability of the ACE inhibitor as shown in the experimental data of the present specification (see for example pages 5-6 of the present specification; Examples 2 and 5, which are compositions prepared in accordance with claim 1, show reduced formation of degradation product as compared to Examples 1, 3 and 4, which are compositions that are not prepared in accordance with claim 1).

Garg is directed to a pharmaceutical composition for sustained release of therapeutically active ingredients to an environment of use. Garg teaches that the composition includes a tablet core, and that the tablet core includes an active ingredient, solubility modifier, osmagents and other conventional excipients. The reference teaches that in their composition, the solubility modulation of the therapeutically active agent, which is weakly acidic in nature, is achieved through the use of the solubility modifier that can be alkalinizing agents, which are in immediate contact with the therapeutically active ingredient and capable of elevating the micro environmental pH of the core above the pKa of the therapeutically active ingredient and thus improving its solubility. Although the reference discloses the possible use of captropil in a list of potential therapeutically active ingredients

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and meglumine in a list of potential alkalinizing agents, nothing in the reference points out any particular significance in using captropil, let alone using any ACE inhibitor along with meglumine.

In particular, the rejection refers to the paragraph starting on line 17 at page 10 for the use of captropil. However, captropil is merely mentioned with a large number of other therapeutically active ingredients having various chemical properties with completely different stabilities in the presence of different excipients.

In addition, the rejection refers to the paragraph starting on line 1 at page 11 for the use of meglumine. However, meglumine is mentioned along with a long list of other compounds, including amino acids, bicarbonate salts, hydroxide salts, salts of gluconic acid, salts of boric acid, salts of citric acid, etc., all of which are used to elevate the micro environmental pH of the core above the pKa of the active ingredient and thereby improve its solubility, as opposed to stabilizing an ACE inhibitor within a stabilized pharmaceutical solid composition. Meglumine also is entirely different from the other listed compounds with respect to its behavior in the presence of an ACE inhibitor, and as such, the reference provides no reason to select meglumine from the various pH elevating compounds and combine it with a drug that undergoes degradation at accelerated rates in the presence of commonly used pharmaceutical excipients such as ACE inhibitors as required by claim 1, nor any reason to expect that meglumine could be combined with an ACE inhibitor and achieve the benefit of superior stability shown in the present specification. Accordingly, claim 1 and the dependent claims therefrom are patentable over Garg for at least these reasons.

Fulbreth does not remedy the deficiencies of Garg. More particularly, Fulbreth is directed to a stable medicinal formulation. While Fulbreth teaches stabilization of ACE inhibitors, and in particular, ramipril, the reference is directed to addressing mechanical stresses during compression by including a polymeric protective film. As such, nothing in Fulbreth suggests combining an ACE inhibitor with meglumine, much less any reason to expect enhanced stability of the ACE inhibitor within a pharmaceutical solid composition under various storage conditions, as demonstrated for example in the experimental work of the specification, could be achieved. Accordingly, claim 1 and the dependent claims therefrom are patentable over Garg and Fulbreth taken alone or together.

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Claims 7-18 are rejected under 35 USC 103(a) as being unpatentable over Garg et al. in view of Fulbreth et al. and further in view of Avrutov et al. (2002/0022646). Applicants respectfully traverse the rejection.

Claims 7-14 and 16-18 depend from claim 1. Avrutov does not cure the deficiencies of Garg and Fulbreth. Accordingly, claims 7-14 and 16-18 are patentable over the references for at least the same reasons as claim 1 discussed above. Applicants do not concede the correctness of the rejection.

Claim 15 is directed to a stabilized pharmaceutical ACE inhibitor composition. Claim 15 requires the composition to include ramipril and meglumine along with at least one of low substituted hydroxypropyl cellulose, pregelatinized starch and magnesium stearate. Advantageously, the composition according to claim 15 show enhanced stability of the ACE inhibitor as shown in the experimental data of the present specification (see for example pages 5-6 of the present specification).

The rejection relies on Avrutov for pregelatinized starch and low substituted hydroxypropyl cellulose as tableting excipients. Applicants again respectfully contend that the rejection improperly uses hindsight in assessing the relevance of the reference. The reference is directed to an economic process for preparing leflunomide in high yield and high purity. However, leflunomide is not relevant to the specific active ingredients indicated by Garg and Fulbreth. Moreover, Avrutov lists low substituted hydroxypropyl cellulose and pregelatinized starch among many other excipients that could be used. Therefore, similar to Garg and Fulbreth, Avrutov fails to provide any teachings that would lead one to combine the specific ACE inhibitor ramipril with meglumine along with at least one of low substituted hydroxypropyl cellulose, pregelatinized starch and magnesium stearate, much less any reason to expect that the superior stability enjoyed by the present invention, demonstrated for example in the experimental work of the specification, could be achieved. Accordingly, claim 15 is patentable over the references taken alone or together.

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In view of the above, favorable reconsideration in the form of a notice of allowance is requested. Any questions or concerns regarding this communication can be directed to the attorney-of-record, Douglas P. Mueller, Reg. No. 30,300, at (612) 455.3804.

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PATENT TRADEMARK OFFICE

Respectfully submitted,

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Dated: August 22, 2008

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